MALARIA, Prevention of[1]

	Drug	Adult dosage	Pediatric dosage
All *Plasmodium* species in chloroquine-sensitive areas[2,3,4]			
Drug of choice:[5,6]	Chloroquine phosphate[7,8]	500 mg (300 mg base) PO once/wk[9]	5 mg/kg base PO once/wk, up to adult dose of 300 mg base[9]
All *Plasmodium* species in chloroquine-resistant areas[2,3,4]			
Drug of choice:[5]	Atovaquone/ proguanil[11]	1 adult tab/d[10]	5-8kg: ½ peds tab/d[10,11] 9-10kg: ¾ peds tab/d[10,11] 11-20kg: 1 peds tab/d[10,11] 21-30kg: 2 peds tabs/d[10,11] 31-40kg: 3 peds tabs/d[10,11] >40kg: 1 adult tab/d[10,11]
OR	Doxycycline[12,13,14]	100 mg PO daily[15]	2 mg/kg/d PO, up to 100 mg/d[15]
OR	Mefloquine[16,17,18]	250 mg PO once/wk[19]	5-10kg: $^1/_8$ tab once/wk[19] 11-20kg: ¼ tab once/wk[19] 21-30kg: ½ tab once/wk[19] 31-45kg: ¾ tab once/wk[19] >45kg: 1 tab once/wk[19]
Alternative:[20]	Primaquine phosphate[12,21]	30 mg base PO daily[22]	0.6 mg/kg base PO daily[22]

1. No drug guarantees protection against malaria. Travelers should be advised to seek medical attention if fever develops after they return. Insect repellents, insecticide-impregnated bed nets and proper clothing are important adjuncts for malaria prophylaxis (Med Lett Drugs Ther 2005; 47:100). Malaria in pregnancy is particularly serious for both mother and fetus; prophylaxis is indicated if exposure cannot be avoided.
2. Chloroquine-resistant *P. falciparum* occurs in all malarious areas except Central America (including Panama north and west of the Canal Zone), Mexico, Haiti, the Dominican Republic, Paraguay, northern Argentina, North and South Korea, Georgia, Armenia, most of rural China and some countries in the Middle East (chloro-quine resistance has been reported in Yemen, Oman, Saudi Arabia and Iran). For treatment of multiple-drug-resistant *P. falciparum* in Southeast Asia, especially Thailand, where mefloquine resistance is frequent, atovaquone/proguanil, quinine plus either doxycycline or clindamycin, or artemether/lumefantrine may be used.
3. *P. vivax* with decreased susceptibility to chloroquine is a significant problem in Papua-New Guinea and Indonesia. There are also a few reports of resistance from Myanmar, India, the Solomon Islands, Vanuatu, Guyana, Brazil, Colombia and Peru (JK Baird et al, Curr Infect Dis Rep 2007; 9:39).
4. Chloroquine-resistant *P. malariae* has been reported from Sumatra (JD Maguire et al, Lancet 2002; 360:58).
5. Primaquine is given for prevention of relapse after infection with *P. vivax* or *P. ovale*. Some experts also prescribe primaquine phosphate 30 mg base/d (0.6 mg base/kg/d for children) for 14d after departure from areas where these species are endemic (Presumptive Anti-Relapse Therapy [PART], "terminal prophylaxis"). Since this is not always effective as prophylaxis (E Schwartz et al, N Engl J Med 2003; 349:1510), others prefer to rely on surveillance to detect cases when they occur, particularly when exposure was limited or doubtful. See also footnote 21.
6. Alternatives for patients who are unable to take chloroquine include atovaquone/proguanil, mefloquine, doxycycline or primaquine dosed as for chloroquine-resistant areas.
7. Chloroquine should be taken with food to decrease gastrointestinal adverse effects. If chloroquine phosphate is not available, hydroxychloroquine sulfate is as effective; 400 mg of hydroxychloroquine sulfate is equivalent to 500 mg of chloroquine phosphate.
8. Has been used extensively and safely for prophylaxis in pregnancy.
9. Beginning 1-2wks before travel and continuing weekly for the duration of stay and for 4wks after leaving.
10. Beginning 1-2d before travel and continuing for the duration of stay and for 1wk after leaving. In one study of malaria prophylaxis, atovaquone/proguanil was better tolerated than mefloquine in nonimmune travelers (D Overbosch et al, Clin Infect Dis 2001; 33:1015). The protective efficacy of *Malarone* against *P. vivax* is variable ranging from 84% in Indonesian New Guinea (J Ling et al, Clin Infect Dis 2002; 35:825) to 100% in Colombia (J Soto et al, Am J Trop Med Hyg 2006; 75:430). Some Medical Letter consultants prefer alternate drugs if traveling to areas where *P. vivax* predominates.
11. Atovaquone/proguanil is available as a fixed-dose combination tablet: adult tablets (*Malarone*; 250 mg atovaquone/100 mg proguanil) and pediatric tablets (*Malarone Pediatric*; 62.5 mg atovaquone/25 mg proguanil). To enhance absorption and reduce nausea and vomiting, it should be taken with food or a milky drink. Safety in pregnancy is unknown; outcomes were normal in 24 women treated with the combination in the 2nd and 3rd trimester (R McGready et al, Eur J Clin Pharmacol 2003; 59:545). The drug should not be given to patients with severe renal impairment (creatinine clearance <30mL/min). There have been isolated case reports of resistance in *P. falciparum* in Africa, but Medical Letter consultants do not believe there is a high risk for acquisition of *Malarone*-resistant disease (E Schwartz et al, Clin Infect Dis 2003; 37:450; A Farnert et al, BMJ 2003; 326:628; S Kuhn et al, Am J Trop Med Hyg 2005; 72:407; CT Happi et al, Malaria Journal 2006; 5:82).
12. Not FDA-approved for this indication.
13. Use of tetracyclines is contraindicated in pregnancy and in children <8 years old. Tetracycline should be taken 1 hour before or 2 hours after meals and/or dairy products.
14. Doxycycline should be taken with adequate water to avoid esophageal irritation. It can be taken with food to minimize gastrointestinal adverse effects.
15. Beginning 1-2d before travel and continuing for the duration of stay and for 4wks after leaving. Use of tetracyclines is contraindicated in pregnancy and in children <8 years old. Doxycycline can cause gastrointestinal disturbances, vaginal moniliasis and photosensitivity reactions.
16. At this dosage, adverse effects include nausea, vomiting, diarrhea and dizziness. Disturbed sense of balance, toxic psychosis and seizures can also occur. Mefloquine should not be used for treatment of malaria in pregnancy unless there is no other treatment option because of increased risk for stillbirth (F Nosten et al, Clin Infect Dis 1999; 28:808). It should be avoided for treatment of malaria in persons with active depression or with a history of psychosis or seizures and should be used with caution in persons with any psychiatric illness. Mefloquine can be given to patients taking β-blockers if they do not have an underlying arrhythmia; it should not be used in patients with conduction abnormalities. Mefloquine should not be given together with quinine or quinidine, and caution is required in using quinine or quinidine to treat patients with malaria who have taken mefloquine for prophylaxis. Mefloquine should not be taken on an empty stomach; it should be taken with at least 8 oz of water.
17. *P. falciparum* with resistance to mefloquine is a significant problem in the malarious areas of Thailand and in areas of Myanmar and Cambodia that border on Thailand. It has also been reported on the borders between Myanmar and China, Laos and Myanmar, and in Southern Vietnam. In the US, a 250-mg tablet of mefloquine contains 228 mg mefloquine base. Outside the US, each 275-mg tablet contains 250 mg base.
18. Mefloquine has not been approved for use during pregnancy. However, it has been reported to be safe for prophylactic use during the second and third trimester of pregnancy and possibly during early pregnancy as well (CDC Health Information for International Travel, 2008, page 228; BL Smoak et al, J Infect Dis 1997; 176:831). For pediatric doses <½ tablet, it is advisable to have a pharmacist crush the tablet, estimate doses by weighing, and package them in gelatin capsules. There is no data for use in children <5 kg, but based on dosages in other weight groups, a dose of 5 mg/kg can be used. Not recommended for use in travelers with active depression or with a history of psychosis or seizures and should be used with caution in persons with psychiatric illness. Mefloquine can be given to patients taking β-blockers if they do not have an underlying arrhythmia; it should not be used in patients with conduction abnormalities.
19. Beginning 1-2wks before travel and continuing weekly for the duration of stay and for 4wks after leaving. Most adverse events occur within 3 doses. Some Medical Letter consultants favor starting mefloquine 3 weeks prior to travel and monitoring the patient for adverse events, this allows time to change to an alternative regimen if mefloquine is not tolerated.
20. The combination of weekly chloroquine (300 mg base) and daily proguanil (200 mg) is recommended by the World Health Organization (www.WHO.int) for use in selected areas; this combination is no longer recommended by the CDC. Proguanil (*Paludrine* – AstraZeneca, United Kingdom) is not available alone in the US but is widely available in Canada and Europe. Prophylaxis is recommended during exposure and for 4 weeks afterwards. Proguanil has been used in pregnancy without evidence of toxicity (PA Phillips-Howard and D Wood, Drug Saf 1996; 14:131).

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MALARIA, Prevention of (continued)

21. Primaquine phosphate can cause hemolytic anemia, especially in patients whose red cells are deficient in G-6-PD. This deficiency is most common in African, Asian and Mediterranean peoples. Patients should be screened for G-6-PD deficiency before treatment. Primaquine should not be used during pregnancy. It should be taken with food to minimize nausea and abdominal pain. Primaquine-tolerant *P. vivax* can be found globally. Relapses of primaquine-resistant strains may be retreated with 30 mg (base) x 28d.

22 Studies have shown that daily primaquine beginning 1d before departure and continued until 3-7d after leaving the malarious area provides effective prophylaxis against chloroquine-resistant *P. falciparum* (JK Baird et al, Clin Infect Dis 2003; 37:1659). Some studies have shown less efficacy against *P. vivax*. Nausea and abdominal pain can be diminished by taking with food.

*Information provided by The Medical Letter. For a copy of the entire **Drugs for Parasitic Infections** article, go to: www.medicalletter.org/parasitic_cdc*

MANUFACTURERS OF DRUGS USED TO TREAT PARASITIC INFECTIONS

albendazole – *Albenza* (GlaxoSmithKline)
Albenza (GlaxoSmithKline) – albendazole
Alinia (Romark) – nitazoxanide
AmBisome (Gilead) – amphotericin B, liposomal
amphotericin B – *Fungizone* (Apothecon), others
amphotericin B, liposomal – *AmBisome* (Gilead)
Ancobon (Valeant) – flucytosine
§ *Antiminth* (Pfizer) – pyrantel pamoate
• *Aralen* (Sanofi) – chloroquine HCl and chloroquine phosphate
§ artemether – *Artenam* (Arenco, Belgium)
§ artemether/lumefantrine – *Coartem, Riamet* (Novartis)
§ *Artenam* (Arenco, Belgium) – artemether
§ artesunate – (Guilin No. 1 Factory, People's Republic of China)
atovaquone – *Mepron* (GlaxoSmithKline)
atovaquone/proguanil – *Malarone* (GlaxoSmithKline)
azithromycin – *Zithromax* (Pfizer), others
• *Bactrim* (Roche) – TMP/Sulfa
§ benznidazole – *Rochagan* (Brazil)
• *Biaxin* (Abbott) – clarithromycin
§ *Biltricide* (Bayer) – praziquantel
† bithionol – *Bitin* (Tanabe, Japan)
† *Bitin* (Tanabe, Japan) – bithionol
§ *Brolene* (Aventis, Canada) – propamidine isethionate
chloroquine HCl and chloroquine phosphate – *Aralen* (Sanofi), others
clarithromycin – *Biaxin* (Abbott), others
• *Cleocin* (Pfizer) – clindamycin
clindamycin – *Cleocin* (Pfizer), others
Coartem (Novartis) – artemether/lumefantrine
crotamiton – *Eurax* (Westwood-Squibb)
dapsone – (Jacobus)
§ *Daraprim* (GlaxoSmithKline) – pyrimethamine USP
† diethylcarbamazine citrate (DEC) – *Hetrazan*
• *Diflucan* (Pfizer) – fluconazole
§ diloxanide furoate – *Furamide* (Boots, United Kingdom)
doxycycline – *Vibramycin* (Pfizer), others
eflornithine (Difluoromethylornithine, DFMO) – *Ornidyl* (Aventis)
§ *Egaten* (Novartis) – triclabendazole
Elimite (Allergan) – permethrin
Ergamisol (Janssen) – levamisole
Eurax (Westwood-Squibb) – crotamiton
• *Flagyl* (Pfizer) – metronidazole
§ *Flisint* (Sanofi-Aventis, France) – fumagillin
fluconazole – *Diflucan* (Pfizer), others
flucytosine – *Ancobon* (Valeant)
§ fumagillin – *Flisint* (Sanofi-Aventis, France)
• *Fungizone* (Apothecon) – amphotericin
§ *Furamide* (Boots, United Kingdom) – diloxanide furoate
§ furazolidone – *Furozone* (Roberts)
§ *Furozone* (Roberts) – furazolidone
† *Germanin* (Bayer, Germany) – suramin sodium
§ *Glucantime* (Aventis, France) – meglumine antimonate
† *Hetrazan* – diethylcarbamazine citrate (DEC)
Humatin (Monarch) – paromomycin
§ *Impavido* (Zentaris, Germany) – miltefosine
iodoquinol – *Yodoxin* (Glenwood), others
itraconazole – *Sporanox* (Janssen-Ortho), others
ivermectin – *Stromectol* (Merck)
ketoconazole – *Nizoral* (Janssen), others
† *Lampit* (Bayer, Germany) – nifurtimox
Lariam (Roche) – mefloquine
§ *Leshcutan* (Teva, Israel) – topical paromomycin
levamisole – *Ergamisol* (Janssen)
lumefantrine/artemether – *Coartem*, *Riamet* (Novartis)
Malarone (GlaxoSmithKline) – atovaquone/proguanil
malathion – *Ovide* (Medicis)
mebendazole – *Vermox* (McNeil), others
mefloquine – *Lariam* (Roche)
§ meglumine antimonate – *Glucantime* (Aventis, France)
† melarsoprol – *Mel-B*
† *Mel-B* – melarsoprol
Mepron (GlaxoSmithKline) – atovaquone
metronidazole – *Flagyl* (Pfizer), others
§ miconazole – *Monistat i.v.*
§ miltefosine – *Impavido* (Zentaris, Germany)
§ *Monistat i.v.* – miconazole
NebuPent (Fujisawa) – pentamidine isethionate
§ niclosamide – *Yomesan* (Bayer, Germany)
† nifurtimox – *Lampit* (Bayer, Germany)
nitazoxanide – *Alinia* (Romark)
Nix (GlaxoSmithKline) – permethrin
• *Nizoral* (Janssen) – ketoconazole
§ ornidazole – *Tiberal* (Roche, France)
Ornidyl (Aventis) – eflornithine (Difluoromethylornithine, DFMO)
Ovide (Medicis) – malathion
§ oxamniquine – *Vansil* (Pfizer)
§ *Paludrine* (AstraZeneca, United Kingdom) – proguanil
paromomycin – *Humatin* (Monarch); *Leshcutan* (Teva, Israel; topical formulation not available in US)
Pentam 300 (Fujisawa) – pentamidine isethionate
pentamidine isethionate – *Pentam 300* (Fujisawa), *NebuPent* (Fujisawa)
† *Pentostam* (GlaxoSmithKline, United Kingdom) – sodium stibogluconate
permethrin – *Nix* (GlaxoSmithKline), *Elimite* (Allergan)
§ praziquantel – *Biltricide* (Bayer)
primaquine phosphate USP
§ proguanil – *Paludrine* (AstraZeneca, United Kingdom)
proguanil/atovaquone – *Malarone* (GlaxoSmithKline)
§ propamidine isethionate – *Brolene* (Aventis, Canada)
§ pyrantel pamoate – *Antiminth* (Pfizer)
pyrethrins and piperonyl butoxide – *RID* (Pfizer), others
§ pyrimethamine USP – *Daraprim* (GlaxoSmithKline)
Qualaquin – quinine sulfate (Mutual Pharmaceutical Co/AR Scientific)
quinacrine
* quinidine gluconate (Eli Lilly)
§ quinine dihydrochloride
quinine sulfate – *Qualaquin* (Mutual Pharmaceutical Co/AR Scientific)
Riamet (Novartis) – artemether/lumefantrine
• *RID* (Pfizer) – pyrethrins and piperonyl butoxide
• *Rifadin* (Aventis) – rifampin
rifampin – *Rifadin* (Aventis), others
§ *Rochagan* (Brazil) – benznidazole
* *Rovamycine* (Aventis) – spiramycin
† sodium stibogluconate – *Pentostam* (GlaxoSmithKline, United Kingdom)
* spiramycin – *Rovamycine* (Aventis)
• *Sporanox* (Janssen-Ortho) – itraconazole
Stromectol (Merck) – ivermectin
sulfadiazine – (Eon)
† suramin sodium – *Germanin* (Bayer, Germany)
§ *Tiberal* (Roche, France) – ornidazole
Tindamax (Mission) – tinidazole
tinidazole – *Tindamax* (Mission)
TMP/Sulfa – *Bactrim* (Roche), others
§ triclabendazole – *Egaten* (Novartis)
§ *Vansil* (Pfizer) – oxamniquine
• *Vermox* (McNeil) – mebendazole

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- *Vibramycin* (Pfizer) – doxycycline
- *Yodoxin* (Glenwood) – iodoquinol
- § *Yomesan* (Bayer, Germany) – niclosamide
- *Zithromax* (Pfizer) – azithromycin

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* Available in the US only from the manufacturer.

§ Not available commercially. It may be obtained through compounding pharmacies such as Panorama Compounding Pharmacy, 6744 Balboa Blvd, Van Nuys, CA 91406 (800-247-9767) or Medical Center Pharmacy, New Haven, CT (203-688-6816). Other compounding pharmacies may be found through the National Association of Compounding Pharmacies (800-687-7850) or the Professional Compounding Centers of America (800-331-2498, www.pccarx.com).

† Available from the CDC Drug Service, Centers for Disease Control and Prevention, Atlanta, Georgia 30333; 404-639-3670 (evenings, weekends, or holidays: 770-488-7100).

• Also available generically.

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